ANNUAL INVENTION STATEMENT

1. Title.

An Implantable Auxiliary Ventricle

2. Full name of inventor. Adrian Kantrowitz, M.D., 546 East 17th Street, Brooklyn, New York 11219. My official title is Director of Surgical Services, Maimonides Hospital of Brooklyn, 4802 Tenth Avenue, Brooklyn, New York 11219, and Professor of Surgery, State University of New York Downstate Medical Center, 450 Clarkson Avenue, Brooklyn, New York 11203.

The auxiliary ventricle was developed with the assistance of several research associates including Tetsuzo Akutsu, M.D., and in collaboration with the Avco-Everett Research Laboratory. Dr. Akutsu resides at 180 East 17th Street, Brooklyn, New York 11226, and is Director of the Division of Experimental Surgery at Maimonides Hospital, and Assistant Professor, State University of New York Downstate Medical Center, 450 Clarkson Avenue, Brooklyn, New York 11203.

The Avco-Everett Research Laboratory is located at 2385 Revere Beach Parkway, Everett, Massachusetts.

3. Name and address of facility. The surgical research laboratory where the auxiliary ventricle was first developed is located in the Edward Neimeth Institute for Medical Research, 4802 Tenth Avenue, Brooklyn, New York.

4. Contribution of the facility to the discovery. I am a full-time employee of Maimonides Hospital. My salary is drawn entirely from hospital funds although a substantial portion of my time is devoted to research.

Dr. Akutsu has been associated with this research since he joined the Maimonides Hospital Surgical Research Laboratory in June, 1964. His salary was derived entirely from Public Health Service Grant HE-06510 until Sept. 1, 1965, and since that time, partially from Grant HE-09934 as well. The Edward Neimeth Institute's contribution includes use of laboratory animal quarters, operating rooms, offices, machine shop and an electronics laboratory.

5. Patent policies of facility. Article 7 of the By-laws of Maimonides Hospital states the following patent policies:

> "All inventions, discoveries, and improvements made by any person in the employ of the Corporation or while receiving any compensation for his services or while using any of the facilities of the Hospital, shall be the property of the corporation to be used by it for the purposes of furthering the medical sciences."
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> "The Board of Trustees may, however, permit the discoverer or the inventor to participate in the income, if any, from the discovery of the invention. The provisions of this Article may be waived by the Board of Trustees."

6. Name and address of any other organization(s) contributing to discovery. The Avco-Everett Research Laboratory, 2385 Revere Beach Parkway, Everett, Massachusetts, is the only other organization involved in this discovery.

7. Contribution of the organization(s) in men, money, facilities. The Avco-Everett Research Laboratory's collaboration with this project began in 1962. Their contribution to the device was to the design of the power supply and timing circuit. This work, while undertaken in collaboration with us, was done at their facility in Everett, Massachusetts. Questions regarding the number of men and financing can be referred to Avco-Everett.

8. Patent policies of these organizations. Patent policies of the Avco-Everett Research Laboratory may be obtained directly from the Avco Company.

9. Detailed description of the invention. The electronically controlled prosthesis, or auxiliary ventricle, consists of a flexible silicone rubber bulb in a firm case of the same contour. It is connected by cuffs of Dacron arterial graft to the ascending and descending aorta, paralleling the aortic arch. Two electrodes pick up the R wave of the ECG from the left ventricle triggering a solenoid valve that controls the application of compressed air from an electronic timer to drive the unit. The time delay--before air is sent into the unit--is determined while left ventricular and central aortic pressure are observed on an oscilloscope. The

device hugs the mediastinum and is close to the aortic root. It contracts in series with the physiologic left ventricle, decreasing systolic pressure and thus reducing this chamber's work. Aortic pressure is increased during diastole, providing normal peripheral perfusion and increasing coronary flow. Other sites in the thoracic and abdominal aorta have been explored. The U-shape occupies less space in the left chest and minimizes the risk of cuff kinking. Blood flows in a smooth curve from the aortic root through the proximal cuff to the auxiliary ventricle lending effective hemodynamic support. When the power source is turned off, blood flows through the device which is now merely acting as a valveless shunt from the ascending to the descending aorta. An end-to-side anastomosis permits perfusion of the cranial and caudal areas. (See three attached figures)

Detailed description of the timing circuit and driving mechanism can be obtained from the Avco-Everett Research Laboratory.

10. Objectives, advantages, and uses of discovery. This intracorporeal, avalvular controllable auxiliary ventricle, or booster heart, offers assistance to the failing left heart. We feel that a device based on this principle will shortly be developed for clinical use, offering patients with myocardial insufficiency either prolonged or intermittent assistance.

11. Your opinion of the importance and usefulness of the discovery: In United States and elsewhere. Pathometric studies of the incidence of heart disease in man have been published widely both in the United States and elsewhere, i.e., "a National Program to Conquer Heart Disease, Cancer and Stroke", U.S. Government Printing Office, 1965, and "World Health Organization Statistics Annual, Volume I: Vital Statistics and Causes of Death," W.H.O., May 1965. Because this incidence is high throughout the world (in the United States it is estimated that of the nearly one million cardiovascular-renal deaths, 54.8%, suffer from arteriosclerotic heart disease including coronary disease), this discovery can be important and useful to any patient who is an appropriate candidate for such assistance. For a further explanation of its usefulness, see Item 10.

12. Your personal desires in applying for a patent on the discovery. Development in the public interest.

13. Reasons, if any, why publication would not be adequate to insure the availability of the discovery to the public. There are numerous publications which should insure priority and availability to N.I.H.

14. Brief statement of how the invention was conceived, its reduction to actual practice, and the dates of these events.

For many years I have been engaged in studies undertaken to develop a workable system that would diminish significantly the left ventricle's work of perfusing blood throughout the body of patients with myocardial insufficiency.

As a Public Health Service Cardiovascular Research Fellow (a) at Western Reserve University working with Dr. Carl J. Wiggers, I began the essential studies on the physiology of the heart which led me to consider the construction of an auxiliary ventricle. This pump device is based on a fundamentally different hemodynamic mechanism in which blood is withdrawn from the arterial system during cardiac systole. The same blood mass is returned intra-arterially during diastole.

(a) Supported by a National Heart Institute Traineeship

At Western Reserve University, later at Montefiore Hospital[b] and subsequently at Maimonides Hospital,[c] in collaboration with others, I became engaged in investigations of more effective methods of augmenting arterial and coronary blood flow considering its extreme sensitivity to increase in diastolic pressure.[1,2,3]

First attempts to create a functioning device to share the workload of the damaged myocardium were begun using the motor power of the hemidiaphragm.[d] In these preliminary experiments in dogs, a portion of the diaphragm was wrapped around the aorta and stimulated by electronic circuitry during each diastole. This work in which I was associated with Dr. William M. P. McKinnon[e] was reported to the American College of Surgeons in 1958. We found that while we could utilize these muscle contractions to propel arterial blood peripherally, it only decreased left ventricular work 10-15%, and posed the formidable

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(b) With the support of a grant from the Playtex Park Research Institute.

(c) With the support of USPHS Grant H-3023, Augmentation of Coronary Blood Flow.

(d) With the support of USPHS Grant H-3023 and continued with the support of USPHS Grant HE-05977 (formerly H-4462) Experimental Construction of an Auxiliary Ventricle.

(e) Supported by USPHS Fellowship HF-9063 and Research Fellowship Supply Grant, An Auxiliary Myocardium.

problem of chronic peripheral nerve stimulation. I felt that more effective results could be obtained with the use of a reservoir.[4,5] This led to the idea of a prosthetic device which would function in the arterial tree.

Resolution of three problems was sought: the quality and type of appropriate material, the most effective site for location of the prosthesis, and its potential volume. Consequently, devices in a variety of sizes were implanted in various ways at various sites in the abdominal or thoracic aorta in an attempt to perfect both the prosthesis and the implantation technique.(f)

At that time the bulb was made of Silastic 382 with cuffs of woven Teflon. Compressed air served as the source of energy and we found that the best effects were obtained when the device was placed in the aortic arch bypass position. This intracorporeal unit, the forerunner of the present device, produced aortic counterpulsation. It was reported to the American Society for Artificial Internal Organs in 1963.[6]

Seeking yet more effective devices for long-term assistance, we subsequently altered the design of the

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(f) Work continued with the support of HE-06510 (formerly H-6510) Integrated Electronic Control of Physiologic Systems.

auxiliary ventricle to an ellipsoidal collapsible bulb in a rigid case of like contour, connected by Dacron arterial graft to the aorta. It was inserted in bypass position parallel to the aortic arch.

With this implanted ventricle, continuous aortic perfusion was achieved for 41 hours in conscious, moving dogs, and intermittently for 10 hours a day for 31 [7,8,9,10,11,12] days.

However, clotting and space problems persisted unti the development of the present device. To minimize clotting within the unit, it was constructed of smoothed Silastic 372 in a U Shape, suggested by Dr. Akutsu, which makes the inner bulb sounder hemodynamically while offering the least physical and chemical interference. It occupies as little space as possible in the left chest and is topographically situated to allow normal functioning of all adjacent organs. Close enough for maximum assistance to the left ventricle, it augments arterial and coronary flow, yet interferes minimally with normal physiology when turned off, acting then as a conduit. Offering the possibility of either consistent or intermittent operation, its materials and design minimize thrombus formation. Patency studies up to 14 months indicate the material's durability and inertness to blood over prolonged

periods. Acute and chronic hemodynamic studies show a consistent reduction of left ventricular work and an increase in coronary flow and natural perfusion. The device was first described to the American Society for Artificial Internal Organs in 1965, and before other professional societies.[13,14,15,16,17,18,19]

On February 4, 1966, the auxiliary ventricle was used in a patient suffering from severe intractable chronic congestive failure. The patient succumbed after 24 hours, although hemodynamic studies indicated good functioning of the unit for 18 hours. The full report of the case is being prepared. The unit used was fabricated by the Avco-Everett Research Laboratory from our specifications.

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19. Chaptal, P.-A., T. Akutsu, and A. Kantrowitz: Hemodynamic Effects of a Mechanical Auxiliary Ventricle Following Induced Heart Failure in Dogs. Amer. J. Cardiol. (Submitted for publication.)

15. Brief statement concerning supporting evidence which you may have at hand which may be used as proof of item 14.

All supporting evidence such as notes, drafts, pressure and flow graphs, etc., are on file in the Division of Experimental Surgery of Maimonides Hospital and are available for review.

16. Brief statement on disclosure of the discovery to others. (Give names and professional affiliations of persons or groups to whom you have made a disclosure and the dates of such disclosures.)

Papers relating to this device and its forerunners were presented before the following groups:

1952, 1954, 1958

Surgical Forum, American College of Surgeons

1960

American Society for Artificial Internal Organs
Research Society of America

1961

Third IBM Medical Symposium
Northeast Electronics Research and Engineering Meeting

1962

American Society for Artificial Internal Organs
New York Academy of Sciences
Brookhaven National Laboratory
New York Society for Cardiovascular Surgery
22nd International Congress of Physiological Sciences (Leiden)
Fourth World Congress on Cardiology (Mexico City)

1963

American Society for Artificial Internal Organs
New York Surgical Society
New York Chapter of the American College of Cardiology

1964

Surgical Forum, American College of Surgeons
American Society for Artificial Internal Organs
Rockefeller University Symposium on Electronic Aids in Medicine
Asian Pacific Congress on Cardiology (Kyoto, Japan)
National Academy of Sciences, National Research Council, Conference on Mechanical Devices to Assist the Failing Heart
Orange County Heart Association, Symposium on Heart Disease (Anaheim, California)
New York Heart Association, Scientific Session on Research
Minnesota Heart Association and Mayo Clinic Symposium on Clinical Application of Electronics in Cardiovascular Disease
IEEE 17th Annual Conference, Engineering in Medicine and Biology

1965

American Society for Artificial Internal Organs
Veterans' Administration Regional Office (New York City)
American Association of Operating Room Nurses
New York Society for Thoracic Surgery
IEEE 18th Annual Conference, Engineering in Medicine and Biology
American College of Chest Physicians
Phlebology Society of America
Heart Association of Southeastern Pennsylvania, Fourth National Symposium: Heart Substitutes (Mechanical and Transplant)
Morgagni Society
Hahnemann Medical College and IEEE Symposium, Engineering in the Practice of Medicine
American Institute of Physics
XXIII International Congress of Physiological Sciences (Tokyo, Japan)

1966

American College of Cardiology

In addition to these presentations at professional societies, the device was discussed at the following hospitals:

Leominster Hospital, Massachusetts, The Jewish General Hospital in Montreal, Jewish Chronic Disease Hospital, Newark City Hospital, Englewood Hospital, Coney Island Hospital 7th Annual Memorial Lecture in honor of Dr. Philip Ingram Nash, Brooklyn Hospital, Memorial Hospital, American College of Chest Physicians Workshop, Mt. Sinai Hospital Postgraduate Seminar 14th Annual Meeting (Miami), and before the Research Society of Maimonides Hospital of Brooklyn.

17. Dates, current location, and names of persons present, if any, when you were developing your experimental data.

Dr. Tetsuzo Akutsu and I may be addressed at 4802 Tenth Avenue, Brooklyn, New York.

Dr. P.-A. Chaptal may be reached at Centre Hopitalier et Universitaire, Montpellier, France.

Dr. Franz Gradel may be reached at Chir. Abt., Anna Seiler Haus, Inselsspital, Berne, Switzerland.

Dr. Y. Nose is in Cleveland, Ohio, Department of Artificial Organs, Cleveland Clinic, 2020 East 93rd Street.

Dr. W.H.P. McKinnon is at New York Medical College, Fifth Avenue at 106th Street, New York City.

Dr. M. Schamaun is in the Department of Surgery, Kantonsspital, Zurich, Switzerland.

Dr. A. Lerrick - deceased

Dr. Arthur Kantrowitz may be reached at the Avco-Everett Research Laboratories at 2385 Revere Beach Parkway, Everett, Massachusetts.

The dates of their individual contributions to this research effort appear on the attached list of references.

18. All information, which you have as to the state of the art and such specific information in the art as to which you may be aware, including any publication already made, or public use being made of the art at the time of the discovery. (Give dates, names, and addresses of publishers and/or users.)

The final aim of the intensive research now taking place in many laboratories throughout the world is the development of a permanently implantable cardiac assistance device with a portable power supply. Steps toward achievement of that goal are being taken by many investigators principally utilizing one of two methods of auxiliary heart function: the ventricular bypass procedure or that of diastolic augmentation (arterial counterpulsation). Since 1957, many research efforts have been directed toward attempts to supplant and/or augment cardiac function with a variety of assistance devices. In addition to the research already reported by this investigator and his colleagues (reported in detail in Answer 14) significant achievements were published from the following laboratories:

Dr. Bert K. Kusserow, at the University of Vermont College of Medicine in 1958, reported a small solenoid-driven diaphragm pump placed in the abdomen of dogs.[1] In recent years, he has modified his

techniques and design.[2,3,4]

C. Dennis, D.P. Hall, J. Moreno, and A. Senning at the State University of New York Downstate Medical Center reduced oxygen utilization of the heart using a left ventricular bypass in 1961 and their co-workers, including R.R. Capelletti, and S.A. Weslowski, reported their work in this area in 1962.[5]

Domingo Liotta, C.W. Hall, W.S. Henly, A.C. Beall, Jr., D.A. Cooley, and M.E. DeBakey of Baylor University, Houston, reported their results in carrying out left ventricular bypass perfusion utilizing a pulsatile valved tubular shunt between the left atrium and the descending aorta. This has subsequently been refined considerably and a report on its use in a patient appeared in 1963.[6,7,8]

These efforts referred to have been directed toward the construction and development of methods which could be used for total cardiac replacement or mechanical ventricles operating in parallel with the intact heart.

As we noted in Question 14, the auxiliary ventricle functions in series with the natural heart and is based on the concept of providing elevated levels of diastolic

perfusion pressure together with corresponding lowering of systolic pressure. It was reported first by us in 1958 and 1960. An alternate method of bringing about what are essentially the same hemodynamic changes was later developed at Harvard University by R.H. Clauss, C. Birtwell, et al. in 1961, and in the same year in St. Louis by V.L. William, T. Cooper and associates, in a study of its application in dogs with complete heart block.[9,10]

Also in 1962, D.H. Watkins and associates discussed the development of myocardial augmentation and its clinical application.[11] A later paper by M. Soroff, Birtwell and others from the Tufts-New England Medical School in Boston, reported to the American Association for Artificial Internal Organs, an "improved method of counterpulsation" along these same lines.[12] A system, consisting of a valveless pulsatile plastic shunt of wide bore which bridges the ascending and descending aortic segments, was discussed by us in 1963, 1964, and 1965. (See references on pages 9 and 10)

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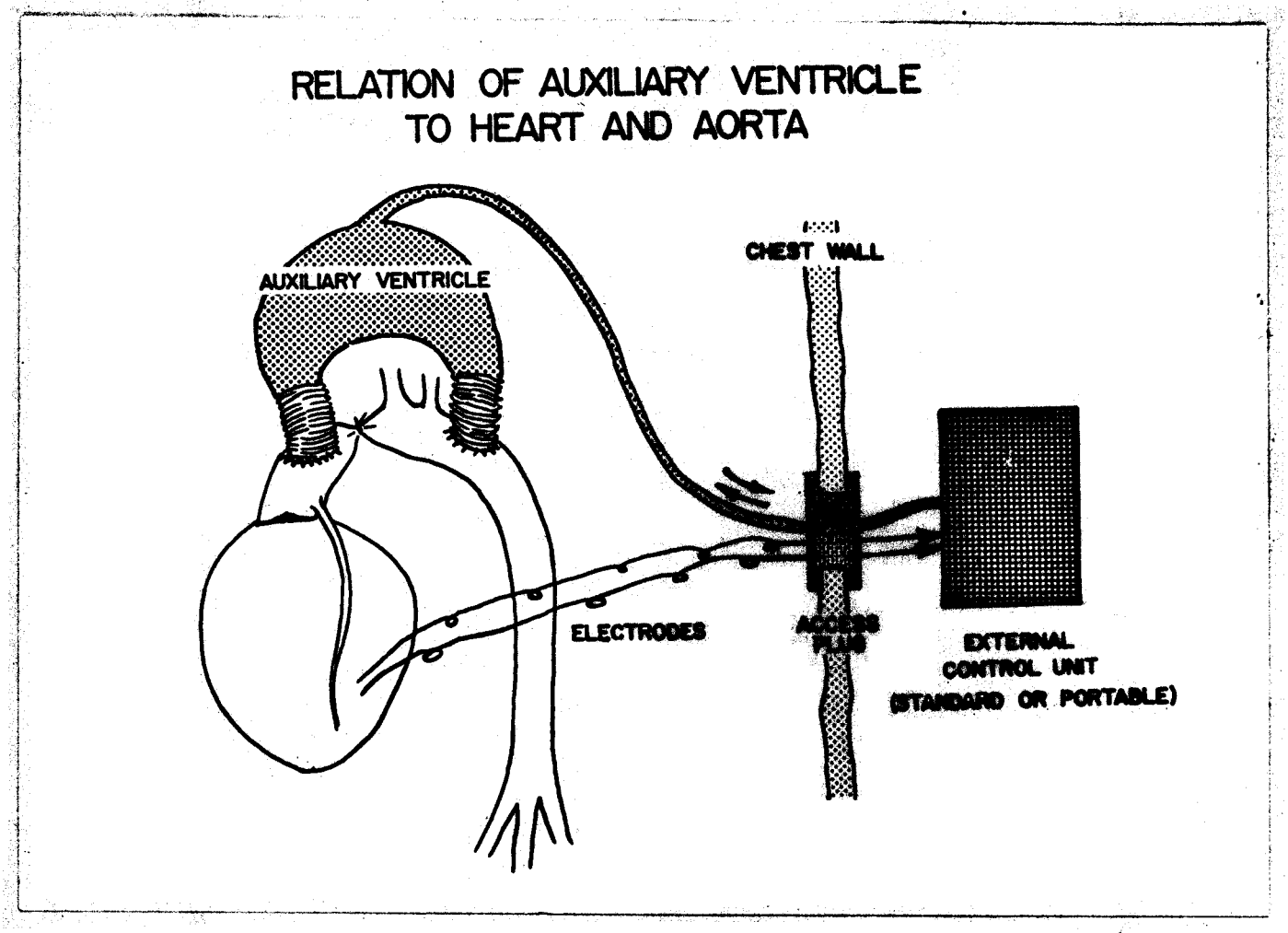

Schematic Diagram of Auxiliary Ventricle System

HE-06510 Integrated Electronic Control of Physiologic Systems
Principal Investigator: Adrian Kantrowitz, M.D. April, 1966